

Claims

1. An isolated nucleic acid molecule which encodes a polypeptide, or sequence variant thereof, wherein said polypeptide is a fragment of the polypeptide sequence represented in Figure 1a or 1b, which fragment is selected from the group consisting of:
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- i) a polypeptide fragment consisting of amino acid residues from about residue 128-224 of the amino acid sequence presented in Figure 1a or 1b;
- 10 ii) a polypeptide fragment consisting of amino acid residues from about residue 128-224 of the amino acid sequence presented in Figure 1a or 1b wherein said sequence has been modified by addition, deletion or substitution of at least one amino acid residue; and
- 15 iii) a polypeptide as defined in (i) and (ii) wherein said polypeptide substantially retains the biological activity of the polypeptide represented in Figure 1a or 1b.
2. A nucleic acid molecule according to Claim 1 wherein said molecule encodes a fragment consisting of amino acid residues from about residue 128-224 of the sequence represented in Figure 1a.
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3. A nucleic acid molecule according to Claim 2 wherein said molecule is isolated from a human.
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4. A nucleic acid molecule according to Claim 1 or 2 wherein said molecule encodes a fragment consisting of amino acid residues from about residue 128-224 of the sequence represented in Figure 1b.
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5. A nucleic acid molecule according to Claim 4 wherein said molecule is

isolated from a nematode.

6. A nucleic acid molecule according to Claim 5 wherein said nematode is of the genus *Caenorhabditis* spp.
- 5 7. A nucleic acid molecule according to any of Claims 1-6 wherein said molecule encodes a polypeptide, or sequence variant thereof, which polypeptide inhibits the activity of a polypeptide represented by the amino acid sequence represented in Figure 2.
- 10 8. A nucleic acid molecule according to any of Claims 1-7 wherein said nucleic acid molecule is a cDNA.
- 15 9. A nucleic acid molecule according to any of Claims 1-7 wherein said nucleic acid molecule is genomic DNA.
10. A polypeptide fragment or sequence variant thereof, encoded by a nucleic acid molecule according to any of Claims 1-9.
- 20 11. A vector comprising a nucleic acid according to any of Claims 1-9.
12. A vector according to Claim 11 wherein said vector is an expression vector.
13. A cell transformed or transfected with a nucleic acid molecule according to any of Claims 1-9 or a vector according to Claim 11 or 12.
- 25 14. A nucleic acid according to any of Claims 1-9 for use as a pharmaceutical.
15. A polypeptide according to Claim 10 for use as a pharmaceutical.
- 30 16. A nucleic acid or polypeptide according to Claim 14 or 15 further comprises a diluent, carrier or excipient.

17. A transgenic non-human animal comprising a nucleic acid molecule according to any of Claims 1-9.
- 5 18. The use of the polypeptide, or fragment thereof, according to Claim 10 in a screening method for the identification of agents which inhibit the binding of said polypeptide to p53.
- 10 19. A screening method to identify agents which inhibit the binding of a polypeptide, or fragment thereof, to p53 comprising:
- i) forming a preparation comprising
 - c) a polypeptide according to the invention; and
 - d) a p53 polypeptide, or a fragment thereof consisting of the binding site(s) for the polypeptide in (a);
 - 15 ii) providing at least one agent to be tested; and
 - iii) determining the activity of the agent with respect to the binding of the polypeptide in (a) to the polypeptide in (b).
- 20 20. A method according to Claim 19 wherein said agent is a polypeptide.
21. A method according to Claim 19 wherein said polypeptide is a peptide.
22. A method according to Claim 20 wherein said polypeptide is an antibody or binding part thereof.
- 25 23. A method according to Claim 22 wherein said antibody is a monoclonal antibody.
- 30 24. A method according to Claim 22 or 23 wherein said fragment is a Fab

fragment.

25. A method according to Claim 24 wherein said Fab fragment is selected from the group consisting of: F(ab')₂, Fab, Fv and Fd fragments; and CDR3 regions.

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26. A method according to any of Claims 23-25 wherein said antibody is a humanised.

10 27. A method according to any of Claims 23-25 wherein said antibody is a chimeric antibody.

15 28. An isolated nucleic acid molecule wherein said molecule is isolated from a nematode worm which nucleic acid molecule hybridises a nucleic acid sequence as represented by Fig 1b, wherein said nucleic acid molecule encodes an inhibitor of p53.

29 A nucleic acid molecule according to Claim 28 wherein said molecule hybridises under stringent hybridisation conditions.

20 30. A nucleic acid molecule according to Claim 28 or 29 wherein said nematode worm is of the genus *Caenorhabditis* spp.

25 31. An isolated polypeptide comprising the amino acid as represented in Figure 2b or a variant polypeptide which polypeptide is modified by addition, deletion or substitution of at least one amino acid residue and is an inhibitor of p53.

30 32. A method of treatment of an animal comprising administering an effective amount of a polypeptide according to Claim 10 wherein said effective amount induces the apoptotic activity of p53.

33. A method of treatment of an animal comprising administering an effective

amount of a nucleic acid molecule according to any of Claims 1-9 or a vector according to Claim 11 or 12 wherein said effective amount induces the apoptotic activity of p53.

- 5 34. A method according to Claim 32 or 33 wherein said treatment is of cancer.
35. A peptide comprising an amino acid sequence selected from the group consisting of: DGPEETD; GPEETD; TTLSDG; AEEFGDE; or PRNYFG.
- 10 36. A peptide according to Claim 35 wherein the length of said peptide is at least 6 amino acid residues.
37. A peptide according to Claim 35 wherein the length of said peptide is selected from the group consisting of: is at least 7 amino acid residues; 8, 9, 10, 11, 12,
15 13, 14, 15, 16, 17, 18, 19, or 20 amino acid residues.
38. A peptide according to Claim 35 wherein the length of said peptide is at least 20 amino acid residues; 30; 40; 50; 60; 70; 80; 90; or 100 amino acid residues.
- 20 39. A peptide according to Claim 35 consisting of an amino acid sequence selected from the group consisting of: DGPEETD; GPEETD; TTLSDG; AEEFGDE; or PRNYFG.
40. A peptide according to any of Claims 35-39 wherein said peptide further
25 comprises a plurality of arginine residues.
41. A peptide according to Claim 40 wherein said plurality of arginine residues is at least 2, 3, 4, 5, 6, 7, 8, 9, or 10 arginine residues in length.
- 30 42. A peptide selected from the group consisting of; DGPEETD; GPEETD; TTLSDG; AEEFGDE; or PRNYFG for use as a pharmaceutical.

43. A pharmaceutical composition comprising a peptide selected from the group consisting of: DGPEETD; GPEETD; TTLSDG; AEFGDE; or PRNYFG.
- 5 44. A pharmaceutical composition according to Claim 43 wherein said composition further includes a carrier, diluent or excipient.
45. A pharmaceutical composition comprising at least one peptide according any of Claims 35-42 and at least one anti-cancer agent.
- 10 46. A pharmaceutical composition according to Claim 45 wherein said anticancer agent is selected from the group consisting of: cisplatin; carboplatin; cyclophosphamide; melphalan; carmusline; methotrexate; 5-fluorouracil; cytarabine; mercaptopurine; daunorubicin; doxorubicin; epirubicin; vinblastine; vincristine; 15 dactinomycin; mitomycin C; taxol; L-asparaginase; G-CSF; etoposide; colchicine; derferoxamine mesylate; and camptothecin.
47. A pharmaceutical composition according to Claim 46 wherein said agent is cisplatin.
- 20 48. A pharmaceutical composition according to Claim 46 wherein said agent is doxorubicin.
49. A complex comprising a peptide according to any of Claims 35-42 and an 25 antibody, or binding part thereof.
50. A complex according to Claim 49 wherein said antibody or binding part is a cell specific antibody.
- 30 51. A complex according to Claim 49 or 50 wherein said antibody is a cancer cell specific antibody.

52. A method of treatment of an animal, preferably a human, wherein said animal would benefit from the induction of apoptosis comprising administering an effective amount of a peptide according to any of Claims 35-41.

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53. A method of treatment of an animal, preferably a human, wherein said animal would benefit from the induction of apoptosis comprising administering an effective amount of a composition according to any of Claims 43-48 or a complex according to any of Claims 49-51.

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54. A method according to Claim 52 or 53 wherein said treatment is cancer treatment.

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